State or California

Memorandum

To : Kathy A. Wynn, Registration Specialist
Pesticide Registration Branch

Date : May 30, 1990
Place : Sacramento

Via : John Ross, Senior Toxicologist
Worker Health and Safety Branch

Phone: 5-8474
HSM-90003 **(# assigned after original issuance of memo)**

From : **Department of Food and Agriculture** - Tian Thongsinthusak, Staff Toxicologist
Worker Health and Safety Branch

Subject: PRODUCT NAME: Omite technical, Omite 30W, Omite 6E, and Comite
ACTIVE INGREDIENT: Propargite
COMPANY NAME: Uniroyal Chemical Co., Inc.
I.D. NUMBER: 122609-ER (One of two memoranda)
DOCUMENT NUMBER: 259-113
EPA REGISTRATION NUMBER: 400-0-
TITLE: Summary and dermal absorption for Omite technical, Omite 30W, Omite 6E, and Comite. April 17, 1990.

Uniroyal Chemical Company has submitted the results of a second complete rat dermal absorption study for Omite technical, Omite 30W, Omite 6E, and Comite (Doc. No. 259-113). The first study was previously submitted and the results contained in Document Number 259-094, -095 and 259-014 (1). The second study was conducted by the Department of Toxicology and Animal Metabolism, Ricerca, Inc. The study protocol had been reviewed and commented on by the Worker Health and Safety Branch (WH&S), California Department of Food and Agriculture on August 16, 1989 (2). Part of the protocol was further amended and agreed upon by the WH&S reviewer according to a Uniroyal letter dated September 27, 1989 (3). Upon reviewing the submitted final report, minor modifications were made during the study, such as the storage temperature and method of anesthetizing rats before killing. However, the study was well executed as evidenced from good recoveries of all administered doses.

Three dose levels were used in the second study: 0.05, 0.5 and 5.0 mg/kg approximately equivalent to 1.1, 11.1, and 111.8 µg/cm^2, respectively. Radiolabeled ^{14}C-Omite with purity of 99% was used for low and mid dose by mixing with formulation blank in HPLC grade water before administration. For high doses the ^{14}C-Omite was, mixed with ^{12}C-Omite and formulation blank in HPLC grade water. For Omite technical the dose was diluted in isopropanol:water in the ratio of I to 4 (v/v).

Four male rats (200-249 grams) were used for each exposure period. The dose of Omite was administered to 4 x 2.5 cm2 skin on the back and shoulder. Treated skin area was lightly clipped with electric clippers and demarcated before dose application. The exposed areas were covered with non-occlusive patches to prevent loss of chemical. At the end of the 0 (5 mg/kg only), 2, 4 hour exposure, the treated site was washed with 5% Liquid Ivory

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soap/water and rinsed with water. A total of five washes and rinses was performed. One wash consisted of one soap wash with a single cotton ball and one water rinse with three separate cotton balls soaked in water. At the end of each observation, rats were anesthetized with ether and killed by exsanguination. All samples necessary for the analysis were collected and kept at $-10^{\circ}C$ or lower for analysis. At the end of the 8 and 24 hour exposure, the treated site was also washed and rinsed the same way. These rats were maintained in metabolism cages for 5 days (Omite 6E and Comite) and 21 days (Omite technical and Omite 30W).

Samples for analyses were appropriately prepared, such as dilution or combustion, and radioactivity was analyzed using liquid scintillation counting. Total radioactivity recovered was the sum of the radioactivity recovered from the protective device, non-occlusive patch, skin washes, urine, feces, blood, skin, hair from rat maintained for 5 days or longer, carcass and cage washes; whereas, percent dermal absorption (as percent of administered dose) was the sum of the radioactivity recovered in the carcass, blood, skin, urine, feces, and cage washes (plus hair if rats were maintained for 5 days or longer).

Percent dermal absorption of Omite for different dose levels and formulations are shown in Table 1. Data for a rat (# 111736) exposed to Omite 30W at 0.05 mg/kg for 24 hours was not used toward the determination of dermal absorption. These data were determined as outliers by the contractor according to procedure by W.J. Dixon (Biometrics, 9:74-89, 1953). However, data for a rat (# 112554) exposed to Comite at 0.05 mg/kg for 24 hours was not excluded from the estimation of dermal absorption as suggested by the contractor. Exclusion of this rat data was not justifiable because there was more variation in the radioactivity recovered among 4 rats in this dose group.

Table 1. Twenty-four hour dermal absorption of propargite (Omite technical, Omite 30W, Omite 6E, and Comite) in male rats[a]

Formulation	Dosage[b] mg/kg	Dosage[b] µg/cm^2	% Reported dermal absorption[c]	% Administered dose recovered	% Corrected dermal absorption[d]	% Dermal absorption first study[e]
Omite tech.	0.05	1.1	20.1 ± 3.6	99.0 ± 3.8	20	NS
	0.5	11.1	12.6 ± 4.1	92.0 ± 1.6	15	NS
	5.0	111.8	5.6 ± 1.1	80.4 ± 1.5	7	NS
Omite 30W	0.05	1.1	17.2 ± 0.6	92.9 ± 2.2	19	9
	0.5	11.1	7.0 ± 1.0	88.4 ± 6.8	8	8
	5.0	111.8	8.7 ± 3.5	89.5 ± 7.6	10	3
Omite 6E	0.05	1.1	10.7 ± 2.9	94.8 ± 1.5	11	9
	0.5	11.1	10.6 ± 2.9	97.3 ± 2.3	11	NS
	5.0	111.8	5.9 ± 1.5	94.7 ± 0.3	6	NS
Comite	0.05	1.1	9.1 ± 7.2	93.6 ± 7.0	10	17
	0.5	11.1	5.1 ± 1.0	89.0 ± 2.8	6	16
	5.0	111.8	8.7 ± 1.1	92.8 ± 2.1	9	14

a n=4 for each dose group, except for Omite 30W at 0.05 mg/kg where n=3.

b Dosage (µg/cm2) was calculated based on the average dosage applied to 10 cm2.

c According to final results submitted (CDFA Pest. Reg. Doc. 259-113).

d Corrected dermal absorption = (c x 100)/% administered dose recovered.

e Dermal absorption (1) determined by Worker Health and Safety Branch, CDFA. NS = No Study

Results shown in Table 1 are grouped according to dosages from all formulations and the results are shown in Table 2.

Table 2. Summary: 24-hour dermal absorption ranges of propargite in male rats for all formulations

Dosage mg/kg	Dosage ug/cm^2	Percent dermal absorption (range of means) second study[a]	Percent dermal absorption (range of means) first study[b]
0.05	1.1	10 - 20	9 - 17
0.5	11.1	6 - 15	8 - 16
5.0	111.8	6 - 10	3 - 14

a CDFA Pesticide Registration Document No. 259-113.

b CDFA Pesticide Registration Document No. 259-094, -095 and 259-014.

There were some differences among percent dermal absorption reported in the first study and in this study. For example, percent dermal absorption at 0.05 mg/kg in the first study for Comite II and Omite 30W were 15 and 10, respectively; however, they were 9 (Comite) and 17 (Omite) percent for the second study, respectively. Due to the range of results of the two studies, a higher percent dermal absorption of Omite technical material (20 percent), and the general trend of worker exposure in the proximity of 1-10 ug/cm^2, the Worker Health and Safety Branch has determined that 24-hour dermal absorption of 17 percent as had been previously calculated is appropriate for estimation of absorbed dosages for workers. Dermal absorption studies by nature have inherent variability. These results between studies are remarkably consistent.

We currently do not know enough about the kinetics or peculiarities of foliar transfer to say that one formulation (or the technical) is more representative of the nature of foliar residue.

References:

1. Uniroyal Chemical Co., Inc. Study on dermal absorption of different 14C-Omite formulations by male rats. California Department of Food and Agriculture, Pesticide Registration Document Number 259-095, -095 and 259-014.

2. Thongsinthusak, Tian. Review and comments on dermal absorption protocol of Omite in rats, Project No. 8920B. A letter to W. F. Cummings (Uniroyal Chemical), WH&S, CDFA, August 16, 1989.

3. Parkins, M.D. Study on the dermal absorption of Omite in rats, Project No. 8920B. A letter to Tian Thongsinthusak. September 27, 1989.

cc: Joshua Johnson (1 original, 5 copies)
Robert I. Krieger